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A critical evaluation of the use of the Schiller test in selecting blocks from the uterine cervix in suspected intraepithelial neoplasia

M K Heatley

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SUMMARY

The value of dipping cervical cone biopsy specimens in iodine (the Schiller test) as a method of deciding which areas should be selected for histological examination was assessed. Schiller positive and negative areas were recorded in macroscopic specimen images from fifty specimens of cervix. The results were compared with the histological presence or absence of cervical intraepithelial neoplasia (CIN) or invasive malignancy. In 84% of cases the test was a reliable means of predicting the presence or absence of squamous CIN; in two cases it was positive in association with endocervical adenocarcinoma in situ. A false positive and false negative Schiller's test was present in three cases (6%) each.

Had this method been adopted as the sole means of selecting blocks for histological examination the areas of CIN would have been missed in 6% of cases. Therefore it is not a sound alternative to the submission of all tissue for histological examination.

INTRODUCTION

Since cervical dysplasia does not display any macroscopic abnormality,[1] it is mandatory to submit any cone biopsy specimen excised from a patient with suspected or established intraepithelial neoplasia of the uterine cervix (CIN) in its entirety for histological examination. Whether the specimen is opened at the twelve o'clock position and divided into longitudinal strips as recommended by some authors[2,3,4] or is sliced sagitally beginning from one lateral edge of the specimen[1,5] either yield multiple histological blocks. Even if more than one block is placed in each processing capsule[3] the processing of cervical tissue represents a significant proportion of the workload of any routine diagnostic histopathology laboratory, as cone biopsy is a commonly performed outpatient and inpatient operation. Consequently any procedure which would allow the pathologist to select those blocks which contained the most significant pathological lesion would allow a reduction in both workload and in the cost of processing cone biopsies.

The Schiller test[6] may be used as part of the colposcopic examination of the vagina and cervix.[7,8] This test consists of the application of aqueous iodine to the cervix: normal squamous epithelium stains a deep brown (Schiller negative) whilst areas of ectropion, metaplastic or dysplastic squamous epithelium do not take up the stain (Schiller positive).

In this study the suitability of this technique as a means of selecting blocks containing areas of squamous CIN was assessed. Since it can be applied to formalin fixed tissue the test can be easily accommodated to use in a routine histopathology laboratory.

Department of Pathology, The University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2UL.
M K Heatley, MD, MRCPath, Senior Lecturer in Gynaecological Pathology.

MATERIAL AND METHODS

Fifty consecutive cone biopsies submitted to the pathology department at this institution were dipped in a 5% solution of aqueous iodine and a colour print of the macroscopic specimen image was made using a Sony UP2200 video printer system.[9] The specimen was serially sectioned[1,3] and each block of tissue was placed in a processing cassette which was labelled with a unique identifying letter. The position from which each block originated was marked on the colour print and the presence of a positive or negative Schiller reaction was recorded. An average of six blocks were examined in each case.

The blocks were processed on a Miles Scientific Tissue Tek Vacuum Impregnation Processor 1000 using a standard processing schedule, embedded in high quality paraffin wax, and haematoxylin and eosin stained sections were cut at 5 μm intervals on a Leitz 1512 microtome. These were examined by the same pathologist. The presence of squamous CIN, infiltrative squamous carcinoma or other pathological abnormality in each of the histological sections was recorded and the results compared with the macroscopic findings. The presence of an ectropion or squamous metaplasia on histology was also noted.

RESULTS

In 84% of the 50 cases the use of the Schiller test was a reliable means of predicting the presence or absence of invasive and intraepithelial neoplasia in the ectocervical squamous and endocervical glandular epithelium. The Schiller test was also positive in cases of adenocarcinoma *in situ* and in benign conditions.

However in three cases in which no abnormality of the Schiller test was present, high grade CIN III was detected histologically. This was confined to the endocervical canal. In two cases CIN was present in association with squamous metaplasia. (See table)

TABLE

The type of lesion associated with a positive or negative Schiller's test in fifty consecutive cone biopsies of cervix.

Type of lesion	*Schiller positive*	*Schiller negative*
Ectocervical squamous dysplasia	39	3
Infiltrating squamous carcinoma	1	0
Adenocarcinoma *in situ*	2	0
Squamous metaplasia	2	0
Ectropion	1	0
No pathological lesion identified	0	2

Examination of the midline blocks taken from the 12 and 6 o'clock positions from the anterior and posterior lips provided an accurate assessment of the histological findings in the cervical epithelium in 49 cases. The exception was a case of a small focus of squamous CIN I which was located at the 1 o'clock position. By contrast all three cases of squamous CIN III which were Schiller negative were represented in the midline blocks of cervix.

DISCUSSION

This study indicates that the routine application of aqueous iodine as the sole method of selecting blocks for histology in cone biopsy specimens is of doubtful value due to its occasional failure to detect squamous CIN. Failures were due to dysplasia, confined to the endocervical canal, which could not be detected by visualisation of the ectocervical surface. This represents a significant limitation to the use of this technique as the exclusive means of selecting blocks for histological examination. In two of three cases squamous metaplasia correlating to the Schiller positive areas was identified elsewhere in the specimen. Had this method been used to select blocks for histology, the metaplasia might have been thought to account for the Schiller positive area and a high grade CIN lesion would have been missed. These findings are perhaps not surprising since gynaecologists have identified a high percentage of false positive and false negative cases when this test has been used in clinical practice.[10]

In addition to the identification of CIN lesions the histological examination of all submitted tissue from cone biopsy specimens of the cervix is justifiable since it allows assessment of resection limits and exclusion of invasive malignancy.

Hysterectomy specimens of uterus and cervix are also commonly encountered in most histopathology laboratories and account for 600 specimens in our department annually. Might the Schiller test have a role as a screening test for the detection of unsuspected CIN in hysterectomy specimens where the uterus and cervix were removed for conditions unrelated to cervical disease? The current practice of taking histological blocks from the anterior and posterior lips of the cervix[11] would have generated 100 histological blocks and would have allowed the detection of 98% of the cases of established cervical intraepithelial neoplasia in this series. By contrast, sectioning Schiller positive areas identified by this technique would have generated 161 additional blocks but would have resulted in fewer (94%) cases of CIN being detected. Since the Schiller test is also positive in the presence of squamous metaplasia and ectropion which are frequently identified on hysterectomy specimens, the routine application of the technique would result in the submission of unnecessary additional blocks for histology. Furthermore since it is recognised that Schiller's test may be negative in the presence of an infiltrating carcinoma[6] confining histological sampling to Schiller positive areas could result in invasive carcinomas being missed.

These findings suggest that the routine application of iodine to hysterectomy specimens should not be adopted either as a means of selecting blocks for histological examination in cone biopsy specimens where CIN has already been established or as a screening procedure in hysterectomy specimens, given the possibility that iodine may induce artefactual changes which might be confused with CIN.[12]

Application of the Schiller test to cone biopsy specimens enables the macroscopic identification of dysplastic areas in a high proportion of cases. In a significant proportion of cases however such areas will be missed, so that application of the test would result in some high grade CIN lesions remaining unsampled. It is not therefore a valid alternative to histological examination of all the tissue submitted.

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